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Analysis of current epilepsy treatment guidelines

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ABSTRACT

Introduction: In 2017, the International League Against Epilepsy (ILAE) published a new classification of seizures. The purpose of this publication is to analyze the use of antiepileptic drugs in epilepsy therapy depending on the types of seizures classified according to ILAE 2017.

State of the art: The new basic classification emphasizes mainly the location, where seizures begin in the brain, as the most important criterion to classify epileptic seizures. In focal onset seizures, 1st line of treatment in children is oxcarbazepine, while carbamazepine, levetiracetam, phenytoin and zonisamide is 1st choice in younger adults and gabapentin and lamotrigine in elderly patients. In younger adults valproic acid can be considered as second line treatment. In generalized tonic and atonic seizures carbamazepine, phenobarbital, phenytoin, topiramate, oxcarbazepine and valproic acid can be used both in children and adults. Safe and effective drugs in myoclonic and myoclonic-atonic seizures in all age groups are topiramate and valproic acid. In absence seizures, 1st line treatment in children is ethosuximide (used exclusively in this seizures type) and valproic acid, while carbamazepine, lamotrigine, oxcarbazepine, phenobarbital, phenytoin, topiramate, valproic acid, gabapentin, levetiracetam and vigabatrin are commonly used in adult patients. Non-pharmacological approaches, used in refractory epilepsy, include: surgical resection of the seizure focus, the ketogenic diet, vagus nerve stimulation and responsive neurostimulation.

Summary: The new ILAE classification corresponds well with the old guidelines well, which leads to simplifying and spreading the knowledge about epileptic seizures treatment.

Key words: Epilepsy; antiepileptic drugs; epileptic seizures

1. INTRODUCTION

In 2017, the International League Against Epilepsy (ILAE) published a new classification of seizures. Although the old classification is still used in clinical practice, especially by non-neurologists, it is important to understand how changing perceptions of different types of epileptic seizures and the change of terminology affect the timeliness of recommendations for antiepileptic drug therapy. The purpose of this publication is to analyze the use of antiepileptic drugs in epilepsy therapy depending on the types of seizures classified according to ILAE 2017.

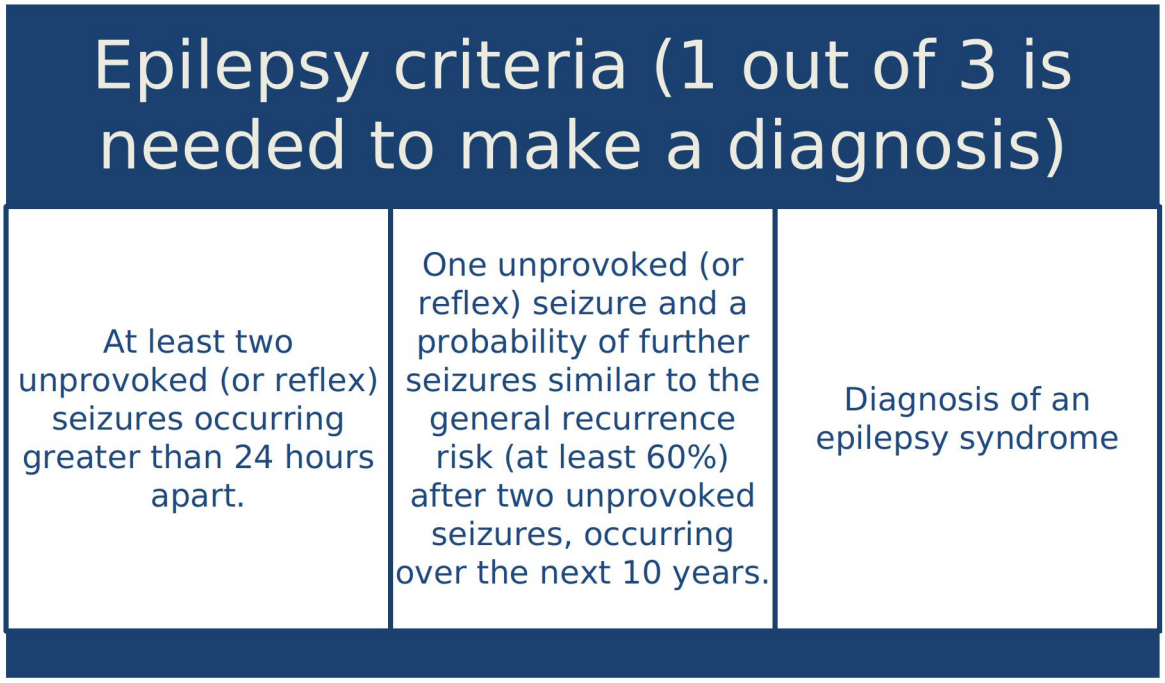


Figure 1. ILAE 2014 revised definition of epilepsy. [2]

1.1. New ILAE Classification

The new basic classification emphasizes 3 key features:

the location, where seizures begin in the brain

the level of awareness of the patient during an epileptic seizure

other features of seizures are also taken into account. [1]

The new names of epileptic seizures, together with the corresponding terms from the old classification, are presented in Table 1.

Table 1. Names of seizures from old classification and the corresponding terms which replaced them.

Old classification	New classification
Simple partial	Focal aware
Complex partial	Focal impaired awareness
Primary generalized	Generalized
Secondary generalized	Focal to bilateral

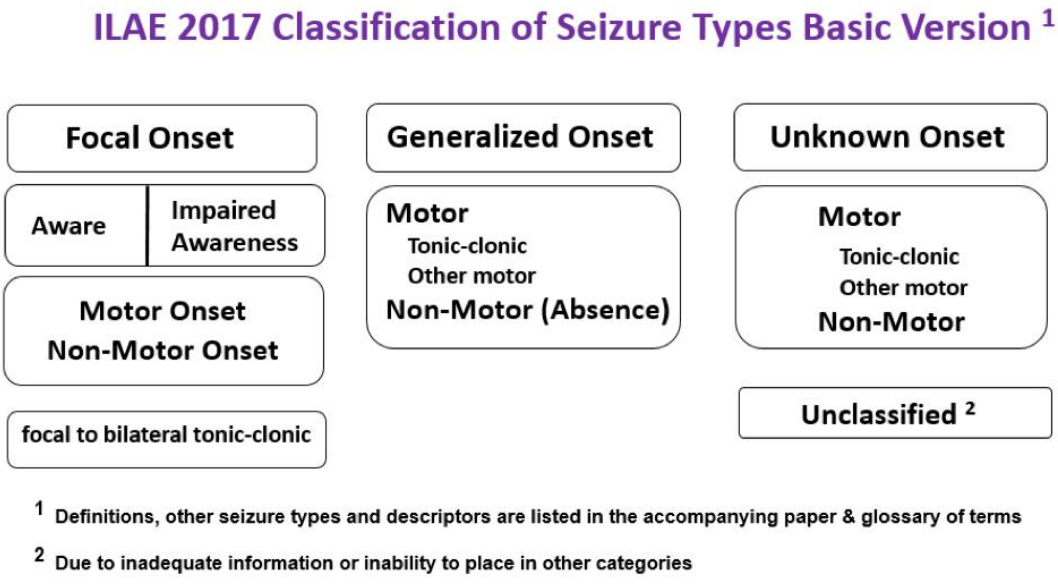


Figure 1. ILAE 2017 Classification of Seizure Types Basic Version [1]

2. RESULTS

The treatment recommendations for different types of seizures were retrieved from various publications, some of which were published before 2017 ILAE guidelines update – in these cases the change of nomenclature was taken into account.

2.1. Focal onset seizures treatment

For the treatment of focal onset seizures in children, the 1st choice medication stays oxcarbazepine. However, depending on clinical conditions, the drugs which are also possible to use are: carbamazepine, phenobarbital, phenytoin, topiramate, valproic acid, vigabatrin, clobazam, clonazepam, lamotrigine, zonisamide.

In adults aged 16-59 years old, the 1st choice treatment are carbamazepine, levetiracetam, phenytoin and zonisamide. The second line drug is valproic acid, while gabapentin, lamotrigine, oxcarbazepine, phenobarbital, topiramate, vigabatrin, clonazepam and primidone are also possible.

In elderly patients gabapentin or lamotrigine should be used first. Carbamazepine, topiramate or valproic acid can be considered either. [1-6]

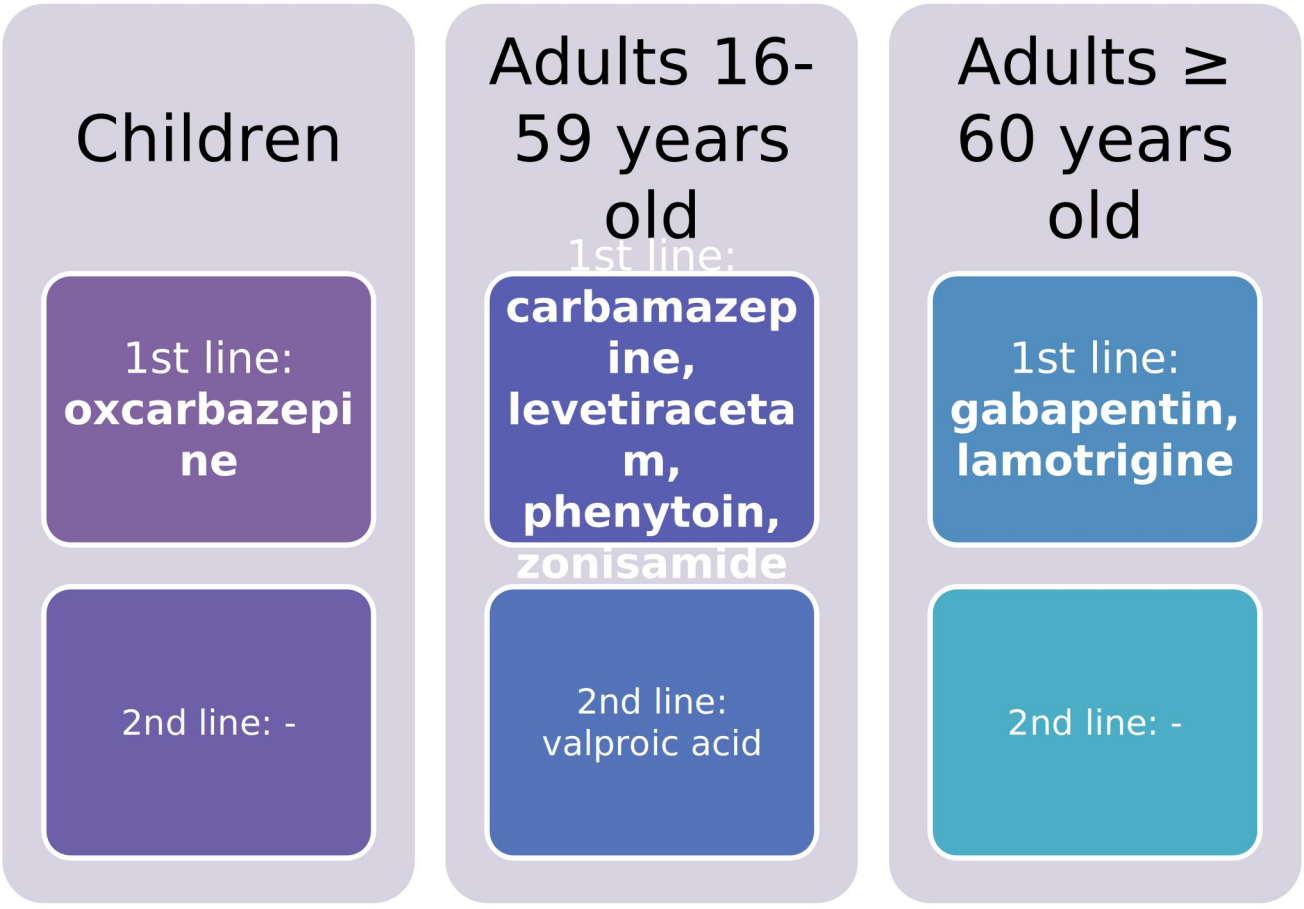


Figure 2. First and second treatment choices in focal onset seizures.

Table 2. Other possible treatment approaches in focal onset seizures depending on the age group

Age group	Other treatment possibilities
Children	**carbamazepine, phenobarbital, phenytoin, topiramate, valproic acid, vigabatrin, clobazam, clonazepam, lamotrigine, zonisamide**
Adults 16-59 years old	**gabapentin, lamotrigine, oxcarbazepine, phenobarbital, topiramate, vigabatrin, clonazepam, primidone**
Adults ≥ 60 years old	**carbamazepine, topiramate, valproic acid**

2.2. Generalized onset seizures treatment

2.2.1. Tonic and atonic seizures treatment

In these kind of generalized onset seizures, the medications that can be used are carbamazepine, phenobarbital, phenytoin, topiramate, oxcarbazepine and valproic acid. Additionally, lamotrigine, gabapentin, levetiracetam and vigabatrin can be also used in adult patients. [1-6]

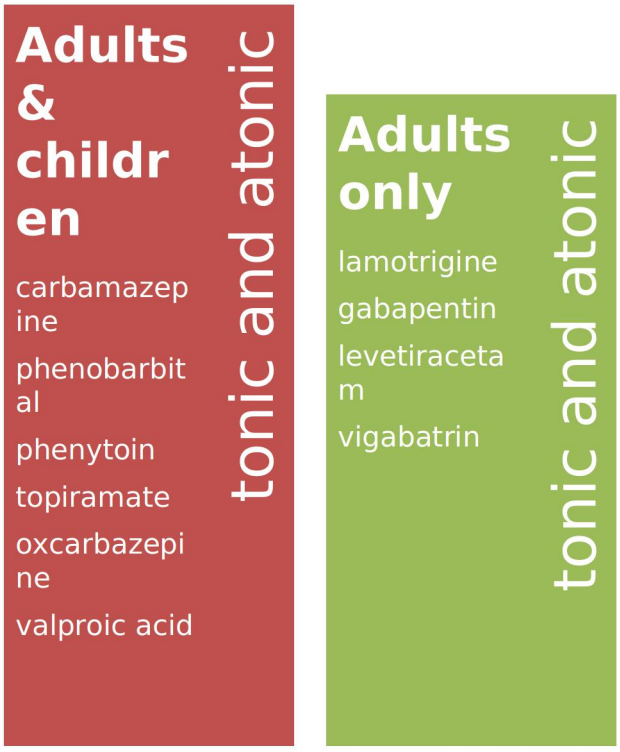


Figure 3. Treatment approaches in tonic and atonic generalized onset seizures.

2.2.2. Myoclonic and myoclonic-atonic seizures treatment

Topiramate and valproic acid can be used either in children and in adults to treat myoclonic or myoclonic-atonic seizures. Moreover, carbamazepine, lamotrigine, oxcarbazepine, phenobarbital, phenytoin,

gabapentin, levetiracetam and vigabatrin are admissible in adults either. [1-6]

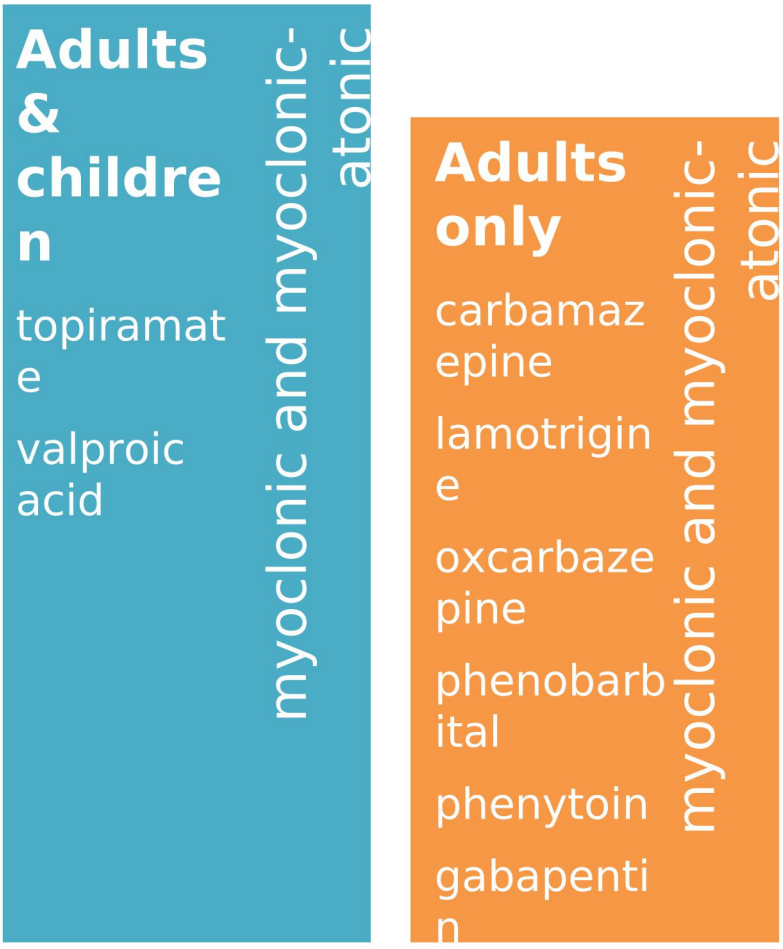


Figure 4. Treatment approaches in myoclonic and myoclonic-atonic generalized onset seizures.

2.2.3. Absence seizures treatment

Ethosuximide and valproic acid are 1st choice treatment for absence generalized onset seizures in children, while lamotrigine is also possible. In adults, numerous medications including carbamazepine, lamotrigine, oxcarbazepine, phenobarbital, phenytoin, topiramate, valproic acid, gabapentin, levetiracetam and vigabatrin are used in this type of epileptic seizures. [1-6]

Figure 5. Treatment approaches in generalized onset absence seizures in children.

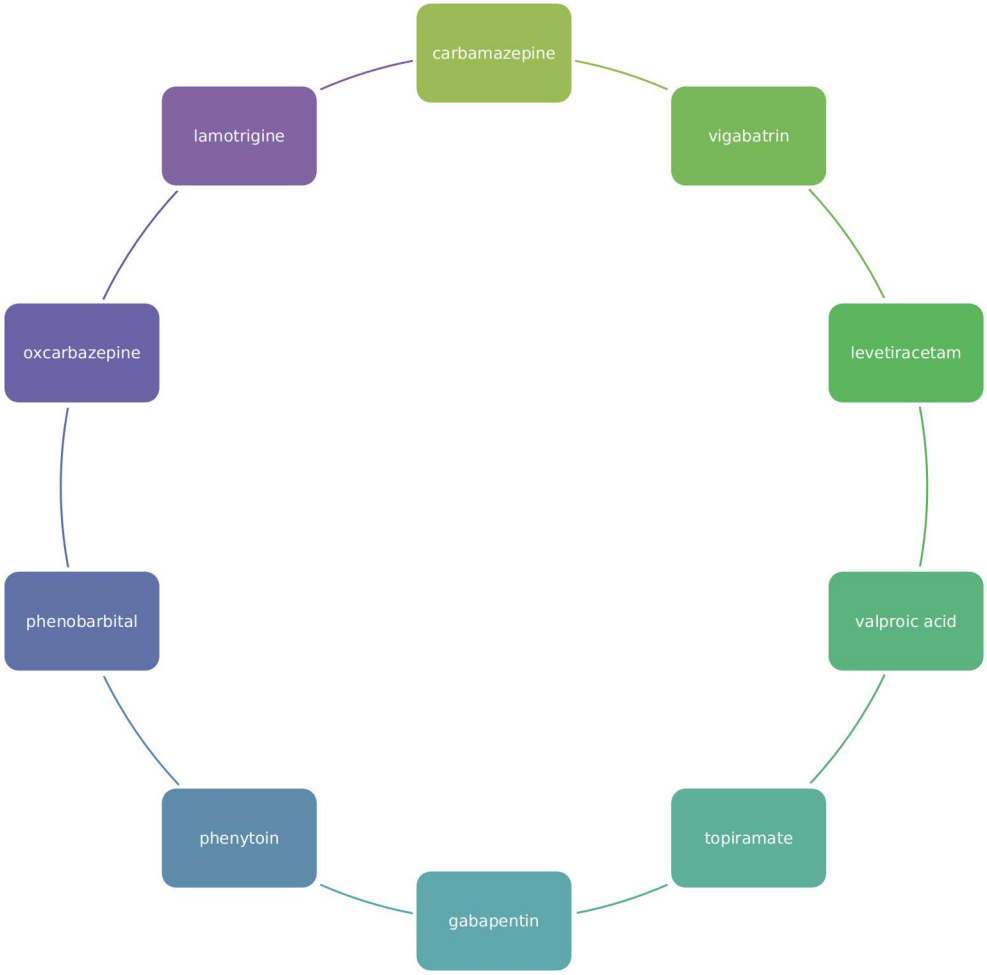


Figure 6. Treatment options in absence generalized onset seizures in adults.

2.2.4. Important limitations

Practically the only antiepileptic drug, that can be successfully used in all kinds of epileptic seizures (both generalized and focal onset) is valproic acid, although it is the 1st line treatment in only some of them.

Carbamazepine, oxcarbazepine, gabapentine, pregabaline, phenytoine and vigabatrin can provoke even more absence and myoclonic attacks (generalized onset seizures), thus they should not be used in individuals presenting these kind of seizures.

Moreover, although carbamazepine and oxcarbazepine are sometimes used in tonic and atonic generalized onset seizures, they are proven to increasing risk of provoking generalized myoclonic and absence seizures therefore caution should be exercised when using these drugs.

Ethosuximide is used specifically for absence seizures treatment in children. [1-6]

2.3. Non-pharmacological approaches

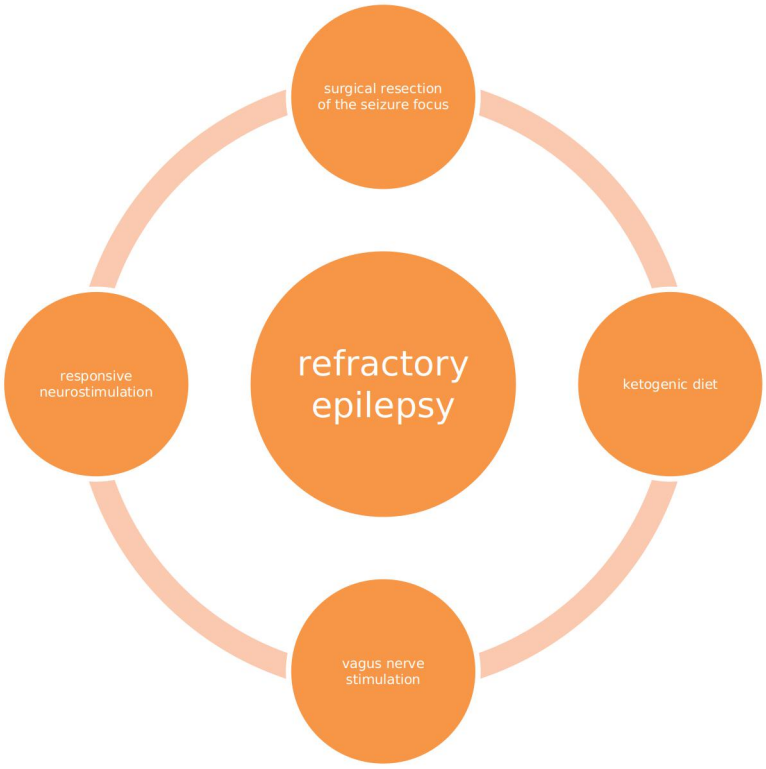


Figure 7. Non-pharmacological approaches in refractory epilepsy.

Possible non-pharmacological approaches in epilepsy treatment, used when medications do not effect in seizures remission, is depicted in Figure 7.

3. CONCLUSIONS

An increasing number of antiepileptic drugs contributes to wider therapeutic options. It is important to match the medication to the patient's seizure accordingly to the new ILAE classification, where the place of initiation of an epileptic seizure in the brain should be considered first. Only then positive treatment effects can be expected, because not all antiepileptic drugs are effective in all types of seizures (although there are those that can be successfully used in almost any type of seizure, e.g.

valproic acid), and in some cases they may even be contraindicated because they may increase the risk of other types seizures. It should be noted that some of the medications that can be successfully used in adults have not been approved for use in children in the guidelines, or are at least are not the first choice therapeutic option. Even despite properly selected treatment, some patients fail to achieve longer periods free of seizures. In case of refractory epilepsy it is vital to remember about non-pharmacological approach, including surgical resection of the seizure focus, the ketogenic diet, vagus nerve stimulation or responsive neurostimulation.

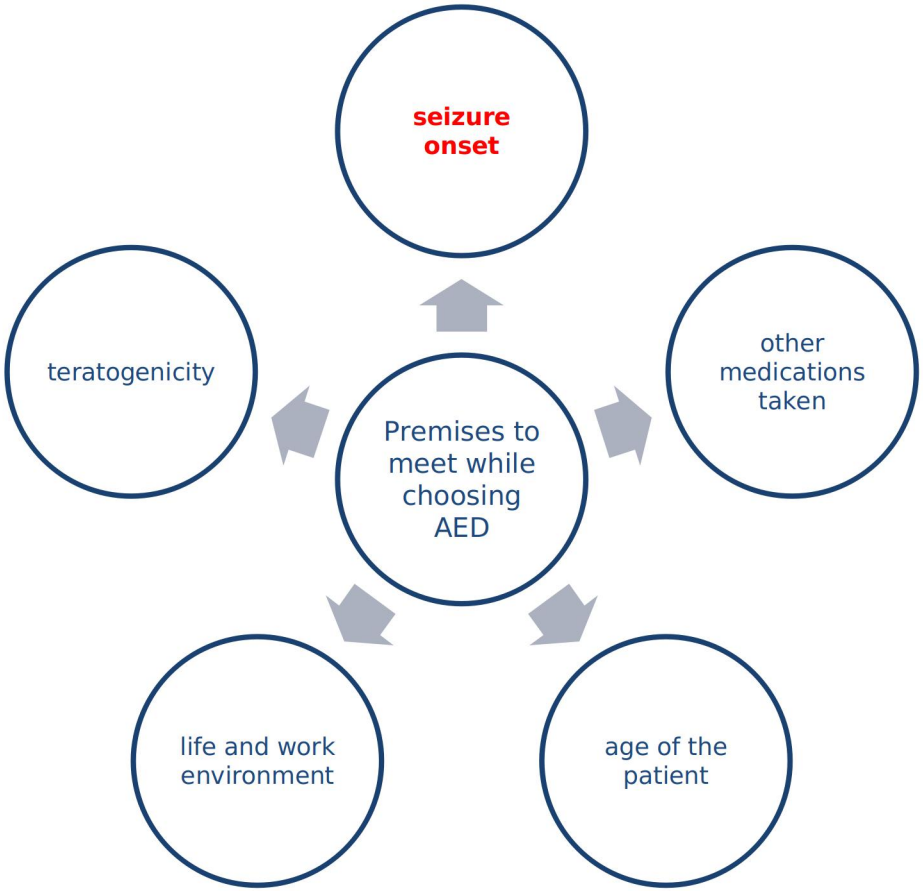
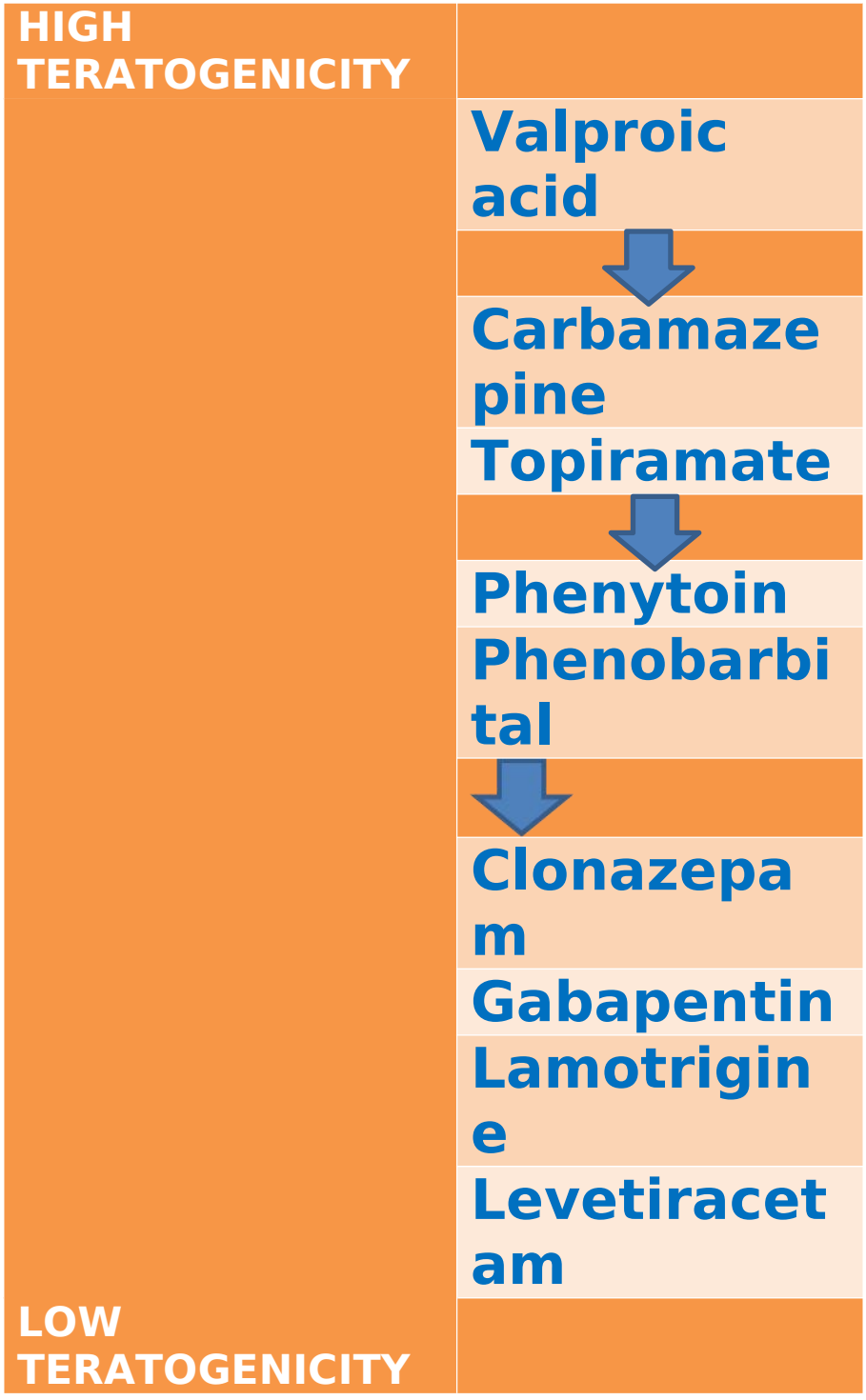


Figure 8. Circumstances that should be taken into account while choosing antiepileptic drugs.

Table 3. Potential teratogenicity of antiepileptic drugs in pregnancy. [6]



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